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Registration Decision RD2012-08

Indaziflam

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Registration Decision for Indaziflam

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is granting full registration for the sale and use of Indaziflam Technical Herbicide, Indaziflam 200 SC Herbicide and Indaziflam 500 SC Herbicide, containing the technical grade active ingredient indaziflam, to control both grassy and broadleaf weeds in pome fruit, stone fruit, tree nuts and grape.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

These products were first proposed for registration in the consultation document[1] Proposed Registration Decision PRD2011-20, *Indaziflam*. This Registration Decision[2] describes this stage of the PMRA's regulatory process for indaziflam and summarizes the Agency's decision and the reasons for it. The PMRA received no comments on PRD2011-20. This decision is consistent with the proposed registration decision stated in PRD2011-20.

For more details on the information presented in this Registration Decision, please refer to 2011-20, *Indaziflam*, which contains a detailed evaluation of the information submitted in support of this registration.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[3] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its conditions of registration. The Act also requires that products have value[4] when used according to label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

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1 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

3 "Acceptable risks" as defined by subsection 2(2) of *Pest Control Products Act*.

4 "Value" as defined by subsection 2(1) of *Pest Control Products Act*"...the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact".

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (e.g., children) as well as organisms in the environment (e.g., those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

What is Indaziflam?

Indaziflam belongs to the chemical class of alkylazines and acts in susceptible plants by inhibiting cell wall biosynthesis. Indaziflam acts only where cellulose synthesis is occuring such as in actively growing meristematic tissues, dividing cells, expanding cells, and growing roots. Fully developed leaves, tissues and plant organs are little affected, if at all, by the compound since cell wall formation has already been completed, and no new cellulose synthesis is required. Indaziflam 200 SC Herbicide and Indaziflam 500 SC Herbicide are selective, residual end-use products that contain the active ingredient indaziflam.

Health Considerations

Can Approved Uses of Indaziflam Affect Human Health?

Indaziflam is unlikely to affect your health when used according to label directions.

Potential exposure to indaziflam may occur through the diet (food and water) or when handling and applying the product. When assessing health risks, two key factors are considered: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g., children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose at which no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when pesticide products are used according to label directions.

In laboratory animals, indaziflam was of low acute oral, dermal and inhalation toxicity. Indaziflam was minimally irritating to the eyes and non-irritating to the skin, and did not cause an allergic skin reaction. Indaziflam 200 SC Herbicide was considered to have a similar toxicity profile to Indaziflam 500 SC Herbicide.

The acute toxicity of the end-use product Indaziflam 500 SC Herbicide containing indaziflam was low via the oral, dermal and inhalation routes of exposure. It was non-irritating to the eyes and skin and did not cause an allergic skin reaction.

Indaziflam did not cause cancer in animals and did not damage genetic material. There was no indication that indaziflam caused damage to the immune system. Indaziflam did not cause birth defects in animals. Health effects in animals given repeated doses of indaziflam included effects on body weight, and the liver, kidney, thyroid, nervous and reproductive systems.

When indaziflam was given to pregnant or nursing animals, there were effects on the developing fetus and juvenile animal. In rat reproductive toxicity studies, effects consisted of decreased body weights, decreased spleen, uterine and brain weights, decreased litter sizes, delayed sexual maturation, neurological effects, and diarrhea. In the rabbit developmental toxicity study, effects consisted of decreased body weights and increased skeletal variations. The effects were observed at doses that were toxic to the mother, indicating that the young do not appear to be more sensitive to indaziflam than the adult animal.

The risk assessment protects against the effects of indaziflam by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

Residues in Water and Food

Dietary risks from food and water are not of concern.

Chronic dietary (food plus water) estimates for the general population and infants less than one year old, the subpopulation that would ingest the most indaziflam relative to body weight,were less than six percent of the acceptable daily intake. Based on these estimates, the chronic dietary risk from indaziflam is not of concern for all population sub-groups. Indaziflam is not carcinogenic; therefore, a chronic cancer dietary exposure assessment is not required. Acute dietary (food and water) estimates for the general population and all population subgroups was less than one percent of the acute reference dose, and is not of concern.

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act.* Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

Residue trials conducted throughout the United States using indaziflam on apples, pears, sweet and tart cherries, peaches, plums, almonds, pecans and grapes, were acceptable. The MRLs for this active ingredient can be found in the Science Evaluation section of this Consultation Document.

Occupational Risks From Handling Indaziflam 200 SC Herbicide and Indaziflam 500 SC Herbicide

Occupational risks are not of concern when Indaziflam 200 SC Herbicide and Indaziflam 500 SC Herbicide are used according to the proposed label directions, which include protective measures.

Farmers and custom applicators who mix, load or apply Indaziflam 200 SC Herbicide and Indaziflam 500 SC Herbicide to orchards, vineyards and nut trees can come in direct contact with indaziflam residues on the skin. Therefore, the label specifies that anyone mixing/loading and applying indaziflam must wear a long-sleeved shirt and long pants, shoes, socks and chemical resistant gloves. The label also requires that workers do not enter treated fields for 12 hours after application. Taking into consideration these label statements, the number of applications and the expectation of the exposure period for handlers and workers, the occupational exposure risk to these individuals is not of concern.

For bystanders, exposure is expected to be much less than that for workers and is considered negligible. Therefore, health risks to bystanders are not of concern.

Environmental Considerations

What Happens When Indaziflam is Introduced Into the Environment?

Indaziflam enters the environment when it is used as a herbicide for control of broadleaf weeds and grasses in pome fruit, stone fruit, tree nuts and grape grown in Eastern Canada and British Columbia.

In the aquatic environment, indaziflam is expected to partition from water to sediment where it is persistent. Soil biotransformation is expected to be the major route of transformation in the environment, with soil persistence ranging from slightly persistent to moderately persistent, depending on soil type. The major transformation products formed in soil include AE 1170437-carboxylic acid and AE 1170437- triazine indanone and AE 1170437-diaminotriazine, all of which are classified as non-persistent, except diaminotriazine which ranges in persistence (from non-persistent to persistent) depending on soil type. Indaziflam is moderately mobile and not expected to leach. In contrast, AE 1170437-diaminotriazine, AE 1170437-carboxylic acid and AE 1170437- triazine indanone are moderately to highly mobile and thus may leach to groundwater, once formed in the soil. Overall, levels of the parent and three transformation products in groundwater are low based on results of water modelling. Based on its low volatility, indaziflam residues are not expected in the air.

Indaziflam does not present a risk to wild mammals, birds, bees, invertebrates, freshwater or marine invertebrates and fish, and amphibians. However, indaziflam does affect terrestrial plants and aquatic plants. Therefore, to protect from the effects resulting from spray drift to non-target terrestrial plants and aquatic plants, buffer zones of 15 metres and 1 metre are required for terrestrial plants and aquatic habitats, respectively. To protect aquatic plants from the potential effects of runoff, a label statement to minimize runoff will be required, as well as hazard based label statements for toxicity to terrestrial and aquatic plants.

Value Considerations

What Is the Value of Indaziflam?

Indaziflam, as a pre-emergence treatment in pome fruit, stone fruit, grapes and tree nuts, provides control of annual grass and broadleaf weeds.

A single application of indaziflam provides effective residual control of annual grasses, including barnyard grass, giant foxtail, green foxtail, Italian ryegrass, large crabgrass, wild proso millet, yellow foxtail and annual broadleaf weeds, including annual sow-thistle, black mustard, common groundsel, field bindweed, lamb's-quarters, prickly lettuce (suppression only), redroot pigweed (suppression only), shepherd's purse, spotted spurge, stork's-bill, white sweet clover and wild mustard in pome fruit (apple, pear), stone fruit (apricot, cherry, nectarine, peach, plum), tree nuts (almond, hazelnut, filbert, walnut, chestnut, Japanese heartnut) and grapes that have been established for at least three full growing seasons in Eastern Canada and British Columbia only.

Indaziflam 200 SC Herbicide and Indaziflam 500 SC Herbicide provides an additional option for herbicide group rotation for controlling both grassy and broadleaf weeds in pome fruit, stone fruit, tree nuts and grape. The use of Indaziflam 200 SC Herbicide and Indaziflam 500 SC Herbicide does not restrict the sequential use of other chemicals of alternate modes of action.

Measures to Minimize Risk

Registered pesticide product labels include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions are required by law to be followed.

The key risk-reduction measures on the label of Indaziflam 200 SC Herbicide and Indaziflam 500 SC Herbicide to address the potential risks identified in this assessment are as follows:

Key Risk-Reduction Measures

Human Health

Because there is a concern with users coming into direct contact with Indaziflam 200 SC Herbicide and Indaziflam 500 SC Herbicide on the skin or through inhalation of spray mists, anyone mixing, loading and applying Indaziflam 200 SC Herbicide and Indaziflam 500 SC Herbicide must wear a long-sleeved shirt and long pants, shoes, socks and chemical resistant gloves. In addition, standard label statements to protect against drift during application and to prevent use in greenhouses were added to the label.

Environment

- Indaziflam 200 SC Herbicide and Indaziflam 500 SC Herbicide cannot be sprayed within 15 metres of susceptible non-target terrestrial plant species, and one metre from aquatic habitats.
- Use of hand-held or backpack sprayer, spot treatment or inter-row hooded sprayer does not require buffer zones.
- Hazard based label statements for toxicity will be required for terrestrial plants and aquatic plants.
- Run-off statements will be required on the label.

Other Information

The relevant test data on which the decision is based (as referenced in PRD2011-20, *Indaziflam* are available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa). For more information, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra.infoserv@hc-sc.gc.ca).

Any person may file a notice of objection[5] regarding this registration decision within 60 days from the date of publication of this Registration Decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the Pesticides and Pest Management portion of the Health Canada's website (Request a Reconsideration of Decision, www.hc-sc.gc.ca/cps-spc/pest/part/protect-proteger/publi-regist/index-eng.php#rrd) or contact the PMRA's Pest Management Information Service.

[5] As per subsection 35(1) of the *Pest Control Products Act*.